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10/553,585	01/13/2006	Robert S. Foote	DC0261US.NP	1514

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MARLTON, NJ 08053

EXAMINER
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COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

NOTIFICATION DATE	DELIVERY MODE
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02/06/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

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poreilly@licataandtyrrell.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/553,585	<b>Applicant(s)</b> FOOTE ET AL.	
	<b>Examiner</b> GARY W. COUNTS	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 4 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/08 has been entered. Currently, claim 4 is pending and under examination.

### ***Claim Objections***

2. Claim 4 is objected to because of the following informalities: line 4 of step (d) the recitation "picrogram" should be --picogram--. Also, line 7 of step (d) the recitation "picrograms" should be --picograms---. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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5. The instant claims recite “the second blood sample as compared to the first blood sample of as small as 9 picograms per milliliter of blood is indicative of cardiac ischemia in the individual”. The specification on page 10, Table 6 discloses change NTproBNP > 5 pg/ml and change BNP > 10 pg/ml. Pages 12-13 of the specification discloses a cutoff point value for diagnosing ischemia can be in the range of 4-10 pg/m., in the range of 4-8 pg/ml or 5 pg/ml. For BNP, a cut point value for diagnosing ischemia can be in the range of 8-16 pg/ml, in the range of 9-12 pg/m., or 9-10 pg/ml for BNP. There is no description in the specification disclosing the second blood sample as compared to the first blood sample of as small as 9 picograms per milliliter of blood is indicative of cardiac ischemia in the individual. Nowhere in the specification does it disclose the second blood sample as compared to the first blood sample of as small as 9 picograms per milliliter of blood is indicative of cardiac ischemia in the individual. Furthermore, none of the originally filed claims recited the limitations in question. Recitation of claim limitations lacking literal or adequate descriptive support in the specification or originally filed claims constitutes new matter.

6. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification on page 3, line 33 – page 4, line 10 discloses that results demonstrate that patients with cardiac ischemia have higher levels of BNP or NTproBNP than patients without cardiac ischemia. Page 7 of the

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specification discloses that both NTproBNP and BNP increased with exercise in all groups. The median incremental rise was almost identical in the healthy volunteers and in the nonischemic patient group. However, the incremental rise in the ischemic group was significantly higher than in the nonischemic group. However, the specification does not disclose any and all natriuretic peptides are involved in cardiac ischemia or provide for the detection of cardiac ischemia, particularly determining pre and post exercise levels of any and all natriuretic peptides and determining cardiac ischemia based on these levels. Kikuta et al., (American Heart Journal, Vol 132, No. 1, Part 1, 1996, pages 101-107) teaches atrial natriuretic peptide (ANP) and teaches that there is no significant differences in plasma levels of ANP among patients with unstable angina as compared with those in patients with stable exertional angina and control subjects (e.g. abstract). Borgya et al (US 20070117156) disclose different natriuretic peptides such as ANP (atrial natriuretic peptide) proANP and CNP (C-natriuretic peptide). Borgya et al teaches that ANP and proANP theoretically would represent suitable markers for the diagnosis of heart failure; in practice they are however, not very stable or only have a short half life in blood, which represents a serious drawback to routine diagnostic measurements (e.g. para 0006). Ebrahim et al (US 20060183681) disclose natriuretic peptides such as CNP and DNP. Ebrahim et al discloses that CNP is of endothelial cell origin; it is found in the brain and cerebrospinal fluid; however, little if any is present in the heart. Ebrahim et al teaches that DNP has been isolated from the venom of the green mamba snake and possesses structural similarity to ANP, BNP and CNP. Prickett et al discloses amino-terminal C-type natriuretic peptide (NT-CNP) and

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discloses that there is a correlation between skeletal growth and the concentrations of the circulating marker (abstract, para. 0010).

7. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for B-natriuretic peptide (BNP) and NTproBNP, does not reasonably provide enablement for any and all natriuretic peptides as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re Wands* USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to a method for detecting cardiac ischemia in an individual suspected of suffering from ischemic cardiovascular disease comprising measuring a level of natriuretic peptide in picograms of natriuretic peptide per milliliter of blood in a first blood sample from an individual suspected of suffering from ischemic cardiovascular disease; subjecting the individual to an exercise stress test with myocardial perfusion imaging wherein a dual isotope, rest-stress protocol is used;

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measuring a level of the natriuretic peptide in picograms of natriuretic peptide per milliliter of blood in a second blood sample from the individual immediately after completion of the exercise stress test; and comparing the actual picogram per milliliter of blood levels of the natriuretic peptide in the first and second blood samples wherein an increase in the actual picogram per milliliter of blood level of the natriuretic peptide in the second blood sample as compared to the first blood sample of as small as 9 picograms per milliliter of blood is indicative of cardiac ischemia in the individual.

The specification fails to teach detecting cardiac ischemia using any and all natriuretic peptides in the instantly recited methods. The specification on page 3, line 33 – page 4, line 10 discloses that results demonstrate that patients with cardiac ischemia have higher levels of BNP or NTproBNP than patients without cardiac ischemia. Page 7 of the specification discloses that both NTproBNP and BNP increased with exercise in all groups. The median incremental rise was almost identical in the healthy volunteers and in the nonischemic patient group. However, the incremental rise in the ischemic group was significantly higher than in the nonischemic group. However, the specification does not disclose any and all natriuretic peptides are involved in cardiac ischemia or provide for the detection of cardiac ischemia, particularly determining pre and post exercise levels of any and all natriuretic peptides and determining cardiac ischemia based on these levels. Kikuta et al., (American Heart Journal, Vol 132, No. 1, Part 1, 1996, pages 101-107) teaches atrial natriuretic peptide (ANP) and teaches that there is no significant differences in plasma levels of ANP among patients with unstable angina as compared with those in patients with stable

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exertional angina and control subjects (e.g. abstract). Borgya et al (US 20070117156) disclose different natriuretic peptides such as ANP (atrial natriuretic peptide) proANP and CNP (C-natriuretic peptide). Borgya et al teaches that ANP and proANP theoretically would represent suitable markers for the diagnosis of heart failure; in practice they are however, not very stable or only have a short half life in blood, which represents a serious drawback to routine diagnostic measurements (e.g. para 0006). Ebrahim et al (US 20060183681) disclose natriuretic peptides such as CNP and DNP. Ebrahim et al discloses that CNP is of endothelial cell origin; it is found in the brain and cerebrospinal fluid; however, little if any is present in the heart. Ebrahim et al teaches that DNP has been isolated from the venom of the green mamba snake and possesses structural similarity to ANP, BNP and CNP. Prickett et al discloses amino-terminal C-type natriuretic peptide (NT-CNP) and discloses that there is a correlation between skeletal growth and the concentrations of the circulating marker (abstract, para. 0010). The examples of the specification are limited to BNP and NTproBNP. Further, as shown above not all natriuretic peptides are indicative of cardiac ischemia. At best the detection of cardiac ischemia can be determined in an individual suspected of suffering from ischemic cardiovascular disease by measuring BNP or NTproBNP in pre and post exercise blood sample from the individual and comparing the levels. Thus, such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to have a high level of predictability, one skilled in the art would have to know that all natriuretic

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peptides are markers for cardiac ischemia and would have to also know that exercise causes changes in these natriuretic peptides.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4, step d, the recitation "the actual pictogram per milliliter of blood" there is insufficient antecedent basis for this limitation.

Claim 4 is vague and indefinite because the recitation "the first blood sample of as small as 9 picograms per milliliter of blood" does not make clear what applicant intends to encompass. It is unclear if the first sample has a value as small as 9 picograms per milliliter of blood or if there is an increase of as small as 9 picograms per milliliter of blood in the second sample as compared to the first sample value.

### ***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section

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351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claim 4 is rejected under 35 U.S.C. 102(e) as being anticipated by Zoghbi et al (US 2004/0243010).

Zoghbi et al disclose determining the level of BNP in samples obtained from a patient. Zoghbi et al disclose that the patient can be suspected of having a coronary artery disease. Zoghbi et al discloses the sample can be a blood sample (e.g. p. 9). Zoghbi et al disclose determining the level of BNP in a sample from the patient prior to exercise to establish a baseline (control) and also teaches determining the level of BNP in a sample from the same patient post exercise (abstract, pgs 9-10, particularly p. 10, Table 1, and Example 7). Zoghbi et al discloses that the levels of the BNP are determined in pg/ml (e.g. see Table 1 and Example 7, lines 1-3 of paragraph 0104). Zoghbi et al disclose that levels of BNP increased from baseline to post-exercise. Zoghbi et al disclose that the exercise stress test can be performed with myocardial perfusion imaging wherein a dual isotope, rest-stress protocol is used (p. 6, para. 0070). Zoghbi et al also disclose that the lowest detectable measurement of BNP can be as low as 5 pg/ml (e.g. Example 2).

Regarding the interpretive "wherein" clause recited in claim1 ("wherein an increase in the actual pictogram per milliliter of blood level of the natriuretic peptide in the second blood sample as compared to the first blood sample of as small as 9 picograms per milliliter of blood is indicative cardiac ischemia in the individual") the clause does not recite any additional active method steps, but simply states a

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characterization or conclusion of the results to those steps. Therefore, the “wherein” clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See *Texas Instruments, Inc. v. International Trade Comm.*, 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) (“A whereby clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim.”). See also *Minton v. National Assoc. of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) (“A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”). Regardless, it is noted that Zoghbi et al teaches the determination of the levels of BNP in pg/ml before and immediately after exercise of the patient and specifically teaches an increase in the levels after exercise (e.g. Table 1 and Example 7, lines 1-3 of paragraph 0104). With respect to the recitation “as small as 9 picograms per milliliter of blood” as instantly recited. It is unclear what applicant intends and further Zoghbi et al discloses the same methods steps and determining the levels in pg/ml and also teaches the detection can be as low as 5 pg/ml and there Zoghbi et al would inherently be able to determine as same as 9 picograms per milliliter in blood.

### ***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Valkirs et al (US 2003/0109420) in view Zoghbi et al (US 2004/0243010 and further in view of DeVito (US 5,249,124).

Valkirs et al disclose a method of diagnosing myocardial ischemia in a patient. (pages 39-40). Valkirs et al disclose determining a level of B-type natriuretic peptide (BNP) in a sample isolated from a patient (p. 7, pgs 22 & 39-40). Valkirs et al disclose that the sample can be obtained after the induction of a stress test (p. 39 1<sup>st</sup> col).

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Valkirs et al disclose comparing the level to a control and correlating the result to myocardial ischemia. Valkirs et al disclose that the control is obtained prior to stress testing (p. 39, 2<sup>nd</sup> col). Valkirs et al disclose that when the test sample is greater than the control that a diagnosis of myocardial ischemia is made.

Valkirs et al differs from the instant invention in failing to teach measuring a level of BNP in picograms per milliliter in the first and second patient samples. Valkirs et al also fails to teach subjecting the patient with an exercise stress test with myocardial perfusion imaging wherein a dual isotope, rest-stress protocol is used.

Zoghbi et al teaches determining the measurement of BNP levels in blood samples of patients. Zoghbi et al teaches immunoassays for determining the quantitative level of BNP (e.g. para 0096, table 1). Zoghbi et al teaches that the immunoassay determines the amount of BNP in picograms/ml and teaches that this immunoassay provides for determining levels as low as 5 pg/ml.

DeVito discloses a stress test with myocardial perfusion studies wherein dual isotope, rest-stress protocol is used. DeVito teaches that dual-isotope study produces two images of the patient's heart and the relationship between the images shows where heart muscle is affected by arteriosclerosis and where it is infarcted (col 2, lines 21-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate immunoassays such as taught by Zoghbi et al for determining the level of BNP in the method of Valkirs et al because Valkirs et al specifically teaches that immunoassay can be used for determining BNP levels (e.g. para 0113, 0114) and Zoghbi et al shows that their immunoassay provides for

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quantitatively determining BNP levels in whole blood and plasma samples as low as 5 pg/ml.

It would have also been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a stress test with myocardial perfusion studies as taught by DeVito into the modified method of Valkirs et al because Valkirs et al is generic with respect to the stress test and DeVito teaches that such studies provides two images of the patient's heart and the relationship between the images shows where heart muscle is affected by arteriosclerosis and where it is infarcted.

Regarding the interpretive “wherein” clause recited in claim1 (“wherein an increase in the actual pictogram per milliliter of blood level of the natriuretic peptide in the second blood sample as compared to the first blood sample of as small as 9 picograms per milliliter of blood is indicative of cardiac ischemia in the individual”), the clause does not recite any additional active method steps, but simply states a characterization or conclusion of the results to those steps. Therefore, the “wherein” clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. See *Texas Instruments, Inc. v. International Trade Comm.*, 988 F.2d 1165, 1171, 26 USPQ2d 1018, 1023 (Fed Cir. 1993) (“A whereby clause that merely states the result of the limitations in the claim adds nothing to the patentability or substance of the claim.”). See also *Minton v. National Assoc. of Securities Dealers, Inc.*, 336 F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003) (“A whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.”). In the instant case, the

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combination of Valkirs et al, Zoghbi et al and DeVito et al perform every active method step and when every active method step has been performed the prior art method is met.

### ***Response to Arguments***

16. Applicant's arguments filed 10/31/08 have been fully considered but they are not persuasive.

17. 102 rejections:

Applicant argues that Zoghbi et al discloses the use of an entirely different endpoint for assessing risk of ischemia in patients. Applicant directs the Examiner's attention to Example 7, page 10 of the Zoghbi et al reference and which states that although BNP increased from baseline to immediately post-exercise in individuals with ischemia as well as those without ischemia.

This is not found persuasive because example 7, page 10, particularly paragraph 0104, lines 5-8 disclose "Neither absolute BNP levels at peak nor the absolute level of rise from baseline to immediate post-exercise differentiated between ischemic and non-ischemic patients". Applicant statement and this passage in Zoghbi et al are not on point because this disclosure is directed to a comparison in non-ischemic patient levels to ischemic patient levels and the currently recited claims are directed to obtaining first and second sample from the same patient and comparing the second level to the first level. As stated above and in the previous office action Zoghbi et al teaches obtaining a first sample from the patient before exercise and post exercise

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and comparing the levels. Further, as stated in lines 1-4 of paragraph 0104 subjects with evidence of ischemia, BNP levels also increased from baseline to immediately post-exercise. Thus, Zoghbi et al is teaching the samples are from the same patient and compared (see also for example table 1, ischemic patients). Further, as stated above the “wherein” clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims.

Applicant further argues that the teaching by Zoghbi et al is the exact opposite of the results of the specification as filed where in Table 6 it is taught that actual increase in the levels of BNP in blood (greater than 9 pg/ml) are diagnostic of ischemia.

First it is noted that Table 6 actually discloses greater than 10 pg/ml. Further, for reasons stated above Zoghbi et al reads on the instantly recited claims.

Applicant further argues that Zoghbi teach away from the method of the present invention which relies on measurement of actual levels of natriuretic peptides in blood, not percent increases as is used by Zoghbi et al. This is not found persuasive because of reasons stated above. Further, Zoghbi et al has performed every active method step and when every active method step has been performed the prior art method is met.

103 rejections:

Applicant argues that a review of the ‘420 application (Valkirs) reveals a key difference between the teachings of the ‘420 application and claim 4 as amended. Applicant argues that the ‘420 application depends on the measurement of absolute thresholds for BNP in blood as is taught at pages 31-32, baseline levels of BNP

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correlate with past medical history, where “higher quartile BNP levels” were associated with cardiovascular diseases that included congestive heart failure, renal function and ECG changes. Applicant further states that the ‘420 patent teaches in various claims that the “threshold BNP level is at least values such as 60 pg/ml or 80 pg/ml.

This is not found persuasive because it appears that applicant is arguing a different embodiment than that which the Examiner has relied upon. It appears that applicant is arguing an embodiment in which Valkirs et al is teaching the comparison to a threshold level (e.g. p 31-32 and claim 3). However, Valkirs et al also specifically teachings that first and second samples are obtained from the same patient and teaches that a control sample is obtained prior to exercise and a sample is obtained post exercise (e.g. page 39, claims 6-15) and the levels are compared to each other.

Applicant argues that nowhere does this patent teach or suggest that an increase in baseline level of BNP in a patient following a stress test of any type of only 9 pg/ml would be useful for diagnosis of ischemia in a patient. This is not found persuasive because as stated above the “wherein” clause is not considered to further limit the method defined by the claim and has not been given weight in construing the claims. Further the combination of Valkirs et al, Zoghbi et al and DeVito et al perform every active method step and when every active method step has been performed the prior art method is met.

### ***Conclusion***

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/  
Examiner, Art Unit 1641

/GAILENE R. GABEL/  
Primary Examiner, Art Unit 1641

2/1/09